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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/922,236	08/02/2001	Tony E. Hugli	SCRIP1460	8664

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EXAMINER	
SAUNDERS, DAVID A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/922,236	HUGLI ET AL.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-34 and 36-72* is/are pending in the application.

4a) Of the above claim(s) *4,13,17,20-24,38 and 47-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-9,11,12,14-16,18,19,25-34,36,37 and 39-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/28/06 has been entered.

Claims 1-9, 11-34, and 36-72 are pending. Claims 1-3, 5-9, 11-12, 14-16, 18-19, 25-34, 36-37 and 39-46 are under examination.

The amendment has entered no new matter.

The amendment has overcome previously stated issues as follows:

The rejection of claims 1-3, 5-9, 11-12, 14-16, 18-19, 25-34, 36-37 and 39-46 under 35 USC 112, 1st paragraph.

The following rejections of record are maintained or modified as follows:

Claims 1-3, 5-9, 11-12, 14, 16, 18-19 stand rejected under 35 U.S.C. 102(a) as being anticipated by Hayashi et al (reference AL on the IDS submitted 12-19-01), as evidenced by Hayashi et al (reference AM on the IDS submitted 12-19-01), both of record, for reasons of record.

As previously stated (action of 11/30/05) there has been no explanation as to why Dr. Craig Jackson is an inventor but not an author of the Hayashi et al reference. Applicant has urged (pg 16) that "the fact that authorship of the abstract and the inventorship of the claimed invention are different, is not cause to reject the invention so long as Applicants have properly declared that the abstract is their work in a 37 C.F.R. Rule 1.132 Declaration." While this statement is true, applicants' problem is that the Rule 1.132 declaration filed on 2/28/06 does not state that "the abstract is their work." Rather, the declaration states that "the above-identified abstract reference is describing Dr. Tony E. Hugli's work and was originated by, or obtained from him" (part 5) and that "Dr Tony E. Hugli alone is the sole inventor of the subject matter of the abstract, and that the other co-author, Joichiro Hayashi, was merely working under Dr Hugli's direction" (part 6). Since the declaration is stating that "Dr Tony E. Hugli alone is the sole

inventor of the subject matter of the abstract", the declaration has failed to state that what is disclosed in the abstract is applicants' work.

Upon reconsideration the following grounds of objection/rejection are newly stated.

The disclosure is objected to because of the following informalities: The disclosure contains amino acid sequences of 4 or more amino acid residues; see, for example "AGLTR" disclosed in para [0013] and [0044]. Full compliance with 37 CFR Rules 1.821 is required.

Claim 16 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 16 contains numerous Markush group members that are not within the scope of a "hepatitis infection" as recited in base claim 1.

Claims 5, 7, 15-16, 18-19, 25-34, 36-37, 39-40, and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships result from the failure of the claim to state how the alpha-2-macroglobulin detection reagent interacts/reacts/binds with/to the components recited in base claim 1 and how the step of claim 5 is related to the purpose and conclusion set forth in base claim 1. The limits of further dependent claim 6 are required to set forth the essential structural cooperative relationships.

In claim 7, "first sample" lacks antecedent basis.

Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural

cooperative relationships are that the claim fails to state how "detecting C3a, C4a, or a combination thereof" relates to the purpose and conclusion set forth in base claim 1.

In claim 16 "other hepatitis virus" is indefinite.

In claim 18 "the substrate" lacks antecedent basis. Dependency from claim 3 would be appropriate.

In claim 25 "the relative quantity" lacks antecedent basis. Recitation of –the level— would be appropriate.

Claims 27-28 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships result from the failure of the claim to state how the peptidase/protease inhibitor detection reagent interacts/reacts/binds with/to the components recited in base claims 25-26 and how the step of claims 27-28 is related to the purpose and conclusion set forth in base claims 25-26. Limits concerning a bound state, as recited in further dependent claim 29, are required to set forth the essential structural cooperative relationships.

Claims 36-37 depend from cancelled claim 35. Dependency from claim 25 would be appropriate.

Claims 39-40 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The omitted structural cooperative relationships are that claim 39 fails to state how "detecting C3a, C4a, or a combination thereof" relates to the purpose and conclusion set forth in base claim 25. Claim 40 fails to state how "determining a relative quantity of C3a and C4a" relates to the purpose and conclusion set forth in base claim 25.

In claim 45 one does not know what the metes and bounds of a "blood-based sample" might be. One does not know if this is limited to a blood sample obtained from a vein or artery (i.e. whole blood or plasma/serum obtained therefrom) or whether this is broader (e.g. including lymphatic fluid, the circulation of which is connected to the blood circulatory system).

Claim 28 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method in which the inhibitor is alpha-2-macroglobulin, C1 inhibitor, or alpha-1- antitrypsin, does not reasonably provide enablement for a method in which the inhibitor is antithrombin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

As the examiner comprehends claim 28, despite its incompleteness (see 112, 2nd supra), the method is intended to be one in which the peptidase/protease inhibitor of base claim 27 is bound to the kallikrein being detected. At Para [0049] applicant teaches that inhibitors that may be bound to kallikrein include alpha-2-macroglobulin, C1 inhibitor, or antitrypsin inhibitor; therein antithrombin is not mentioned. The one exemplification of an assay in which antithrombin (AT) is detected involves the case in which AT III is detected (Example II); therein, at para [0102], applicant teaches that the detected AT III "fell outside the region" (i.e. "the region" of peptidase/kallikrein activity) in Fig. 6. As far as the examiner understands this statement, it teaches that AT III is not bound to the kallikrein. Since the one exemplified antithrombin is not bound to the kallikrein, the examiner does not comprehend how it is possible for an antithrombin to be operative as the inhibitor to be detected in the method of claim 28. Clarification is requested.

Claim 45 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the detection of kallikrein in whole blood or in plasma, does not reasonably provide enablement for the detection of kallikrein in other "blood-based" samples such as serum. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Since serum is obtained from clotted/coagulated blood and since kallikrein is produced from prekallikrein in the clotting process (e.g. see para [0035]-[0036]), one of skill would reasonably expect that the kallikrein level detected in serum does not represent the actual value of kallikrein level in blood or plasma. Applicant's exemplification of detecting kallikrein in anti-coagulated blood samples would not therefore lead one of skill to expect that detecting kallikrein in sera samples would provide any useful data. While base claim

41 does not require that one relate any detected level of kallikrein to a liver disease state, it is to be considered, also, that applicant has failed to teach one how to use what is detected as kallikrein activity level in the case wherein the sample is serum.

Claims 1-2, 7 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Derwent Abstract of JP 59203958 A (of record in IDS of 6/26/02).

The JP publication shows detection of alpha-1-proteinase inhibitor-kallikrein complexes. The assay to detect these involves the use of a protease inhibitor detection reagent (i.e. an enzyme labeled anti- alpha-1-proteinase inhibitor antibody). Acute hepatitis patients show an increased level of alpha-1-proteinase inhibitor-kallikrein complexes in serum. The instant recitation that what is detected is "indicative of liver damage due to hepatitis infection in the subject" carries no patentable weight. Thus instant claim 1 is anticipated.

Instant claim 2 is included because serum and plasma kallikrein are the same. The claim does not require that a plasma sample be assayed; the claim merely requires that what is detected be the same as "plasma kallikrein".

Withdrawn claim 4 would also be anticipated, since the method also uses an antibody against kallikrein, which is a "kallikrein binding agent."

Regarding claim 7, the samples were body fluids from mammals (humans).

Claim 16 is included because the Markush group of hepatitis viruses would include anything exemplified or mentioned in the reference.

Claims 1-3, 5-8 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Derwent Abstract of JP 59203957 A (of record in IDS of 6/26/02).

The JP publication shows detection of alpha-2 macroglobulin-kallikrein complexes. The assay to detect these involves the use of a kallikrein substrate. Hepatitis patients with liver damage show a decreased level of alpha-2-macroglobulin-kallikrein complexes in plasma. The instant recitation that which is detected is kallikrein versus the teaching of the reference that alpha-2- macroglobulin is that which is detected does not render the instant claims different or distinguishable, because in both cases it is the peptidase activity of kallikrein that is detected. Thus instant claims 1-3 and 7-8 are anticipated.

Claim 5 is included because the anti-alpha-2 macroglobulin antibody used by the JP publication serves as an "anti-alpha-2 macroglobulin detection reagent."

Claim 6 is included because the Kallikrein detected is bound to alpha-2 macroglobulin.

Claim 16 is included because the Markush group of hepatitis viruses would include anything exemplified or mentioned in the reference.

Claims 1, 7-8 and 16 are rejected under 35 U.S.C. 102(a) as being anticipated by Derwent Abstract of RU 2155341 C1.

The RU publication shows detection of blood plasma kallikrein. The level thereof is lowered when there is a chronic Hepatitis B infection. Since detection of Kallikrein inherently involves the use of some sort of "kallikrein peptidase detection reagent", instant claims 1, 7 and 16 are anticipated.

Regarding claim 8, it is deemed inherent that the subjects studied were mammals.

Withdrawn claim 13 would be anticipated.

Claims 41-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Svendsen (4,016,042, of record in IDS of 6/26/02).

Svendsen teaches detecting kallikrein activity levels in plasma samples with the use of chromogenic substrates, embodiments of which would correspond to commercially available substrate S2302 (col. 2, lines 50-col. 3, line 68; col. 24, lines 34-59). Applicant has taught that the substrates of Pat. '042 and the commercially available substrate S2302 are useable in the instant invention (para [0013], [0044] and [0088]). The S2302 substrate is a tripeptide having a pNA moiety as the chromogen (para [0013], [0044] and [0088]). thus claims 41-46 are anticipated.

Claims 1-3, 7-8, 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Svendsen (4,016,042).

As noted supra, Svendsen teaches detecting kallikrein activity levels in plasma samples with the use of chromogenic substrates. On the basis that no weight is to be given to relating the

detected interaction of kallikrein and detection reagent (substrate) to a condition of hepatitis infection, the above claims are anticipated.

Claims 1-2 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Svendsen.

Svendsen has been cited supra as anticipating claims 1-2. Svendsen teaches that the substrates are useful for detecting the effect of protease inhibitors upon the activity of kallikrein (col. 2, line 63 and col. 3, line 66). Since any determination of the effect of any inhibitor would involve a comparison against a sample in which there is no inhibitor, the feature of using two portions of a sample, as in claim 18, would have been obvious.

Attached to this action is a corrected copy of Form PTO-1449 filed 6/26/02; the correction involves a change in the date of the last cited foreign patent.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, PhD whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 5/11/06 DAS

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